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10/067,148	02/01/2002	Marie-Cecile Van de Lavoie	271/123	4804

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EXAMINER

KAUSHAL, SUMESH

ART UNIT PAPER NUMBER

1633

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/067,148

**Applicant(s)**

VAN DE LAVOIR ET AL.

**Examiner**

Sumesh Kaushal Ph.D.

**Art Unit**

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 28 November 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 21,26-30 and 41-50 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 41-50 is/are allowed.
- 6) ☒ Claim(s) 21 and 26-30 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_. 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

*Applicant's response filed on 11/28/05 has been acknowledged.*

*Claims 21, 26-30, 41-50 are pending and are examined in this office action.*

*Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306.*

*The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.*

**Claim Rejections - 35 USC § 103**

The rejection of claims under 35 U.S.C. 103(a) 41-50 has been withdrawn in view of applicants remarks and Dr. Etches's sworn declaration that the germ line transmission could not be maintained for ES cell held more than 7 day in culture and only minor somatic contributions could be obtained after 21 days in culture.

Claims 21, 26-30 *stand* rejected under 35 U.S.C. 103(a) as being unpatentable over Pain et al (Development 122:2339-2348, 1996, ref of record), Petite et al (US 5,830,510, 1998) and Gibbins et al (Pro. 4<sup>th</sup> World Congress on Genetics applied to livestock production XVI, 118-122, Edinburg 1990, ref of record), for the same reasons of record as set forth in the office action mailed on 5/23/05.

The instant claims are drawn to a chimeric chicken comprised of progeny of genetically modified embryonic stem cells.

Pain teaches in-vivo differentiation of chicken embryonic stem cells (CEC) obtained from long-term in-vitro culture. Cited art further teaches irradiated cultured CEC obtained from Barred Rock black strain CEC were injected into the subgerminal cavity of stage X White Leghorn recipient embryos, which resulted in the hatching of chimeric plumage phenotypes (see claims 21, 41, 43-44). The cited art further teaches that regardless number of passages more than 50% of the hatched recipient embryos were chimeras with nearly 33% of plumage from donor phenotype (page 2344 col.2 para.2; page 2346, fig-8). The cited art further teaches CEC expressing ECMA-7, SSEA-1 and EMA-1 could be cultured for at least 35 passages i.e. more than 160 days in the presence of LIF, a cytokine (page 2343 col. 1-2, fig-4). Regarding claims 26-30, the cited art teaches that it is well known in the art that cells derived from early chicken blastoderm will contribute to both somatic and germ line when injected into recipient embryos to form chimeras (page 2339, col.2 para.2). The cited art further teaches that long-term cultured CEC were capable of differentiating several lineages, which could be characterized lineage marker specific antibodies (page 2344 col. 1 para. 3). However Pain et al does not teach the genetic modification of embryonic stem cells prior to the injection into the recipient embryo.

Petite teaches veterinary pharmaceutical formulation comprising sustained avian cells in an amount effective to alter the phenotype of an ave wherein the avian cells comprising undifferentiated avian embryonic stem cells (col.8 lines 35-49). The cited art further teaches genetic modification of avian embryonic stem cells by transfecting avian embryonic stem cells with the DNA sequence in vitro (e.g., by electroporation or transformation with a retroviral vector), and then injecting the transfected embryonic stem cells into an egg containing an embryonic bird (col. 4 lines 7-30). The cited art further teaches culturing and maintenance of avian embryonic stem cells for 23 passages which is approximately 2 months (60 days) see col.8, lines 5-9, table-1.

Similarly, Gibbins et al teaches efficient transfer of chicken blastoderm cells and their incorporation into recipient embryos to produce chimeric chickens. The cited art teaches that isolation and culture of pluripotent embryonic stem cells and transfection of these cells with DNA constructs using Lipofectin. The cited art further teaches selection

of stably transfected cells and introduction of the transfected cells into a recipient embryo to generate chimeric birds (page 120, paras 2-3). The cited art further teaches successful construction of chimeric birds from several different donor/recipient line combinations indicating that the technique should have broad applicability across breeds (page 121, para.2).

Thus it would have been obvious to one ordinary skill in the art at the time the instant invention was made to modify the teaching of Pain with Petite and Gibbins by substituting the embryonic stem cells with genetically modified avian embryonic stem cells in order to make chimeric chickens. One would have been motivated to do so to make transgenic birds by cross breeding the chimeric chickens. One would have a reasonable expectation of success, since genetic modification, long term culture of embryonic stem cells and making chimeric birds using embryonic stem cells has been routine in the art. Thus the invention as claimed is *prima facie* obvious in view of cited prior art of record.

***Response to Arguments and Dr. Etches Declaration***

Applicant's arguments and Dr. Etches sworn Declaration filed 11/28/05 had been fully considered.

The Dr. Etches's declaration states "*Although the work described in the Pain et al. paper involved long-term cultures of chicken embryonic stem cells, none of this work resulted in the successful generation of chimeras from embryonic stem cells or their progeny held in culture for longer than 19 days. This fact is reflected in the legend to Figure 8 of the Pain et al. paper where the authors recited the longest culture period from which chimeric birds have been generated*". The declaration further states that "*Given that the longest period of time in which cells had been maintained in culture and demonstrated to have the capability to contribute to the somatic tissue of a chimeric chicken was 19 days according to the Pain et al. paper, it would not have been expected that the chicken ES cells could be maintained in culture for a period of time long enough to be transformed such that a transgene was stably integrated into the genome of the cells while maintaining the ability of the cells to colonize somatic tissues and differentiate into specialized cell types when these transformed chicken embryonic stem cells were injected into a recipient*" (see declaration page 2). In view of Dr. Etches Declaration the applicant

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concluded that the ability of Pain, Etches et al was restricted to 7 days and ability to make somatic chimeras was restricted to 21 days. The applicant admits that Pain, Etches et al clearly teaches that *"Cells were collected from cultures after 1-3 passages. 100-500 cells were injected into the subgerminal cavity of irradiated stage X White Leghorn recipient embryos. Several of the grafted embryos hatched, some of which exhibited a chimeric plumage phenotype (Fig 8). Regardless of the number of passages, more than 50% of the hatched recipient embryos were chimeras with nearly 33% of the plumage color from donor phenotype."* (See remarks page 6). Based upon the declaration the the applicant concluded that chimeras could not be made from cells that had been in cultured for longer than 19 days as is explicitly stated in the caption to Figure 8 of the reference. (See also Etches Affidavit para 5-6, 9).

Regarding making chimeras from cultured embryonic stem cells the applicant concluded that *Pain, Etches et al. (1996) paper teaches a culture containing cells which could produce chimeras, within 3 passages, when maintained in culture for 19 days or less. The applicant admits that for a short period of time (i.e. up to 19 days), these cells could make somatic chimeras, and for 7 days, these cells could make germ line chimeras. However, after longer periods in culture, they could make neither somatic not germ line chimeras. See remarks page 9, para. 3.* Regarding Petite (US 5,830,510) the applicant argues that even though the cited art suggests the genetic modification of ES in order to make chimeric birds, the citation of Petite is not evidence to support a prima facie basis under 35 USC 103. The applicant further argues that Petite does not teach long-term culture of transformed ES cells (Remarks page 10, para. 2). Regarding Gibbons the applicant argues that the cited art does not teach the use of embryonic stem cell lines. The applicant concluded that prior to the present invention the genetically modified ES necessary to make the chimeric birds of inventions did not exist, therefore the invention as claimed is not obvious. The applicant further argues that the present invention satisfies long-felt need in the art and overcomes prior failed attempts by others. The applicant argues that as recently as 2004 Petite et al did not report the creation of chimera using ES cultured longer than 20 days. The applicant argues that invention as claimed is not obvious because others fail to achieve the claimed invention.

The rejection of claims 41-50 has been withdrawn in view of applicants remarks and Dr. Etches's sworn declaration that the germ line transmission could not be maintained for ES cell held more than 7 day in culture and only minor somatic contributions could be obtained after 21 days in culture.

However, regarding claims 21 and 26-30 the applicant's arguments are found NOT persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The combined teaching of prior art of record clearly suggest that a chimeric chicken composed of progeny of genetically modified embryonic stem cells is obvious. As stated earlier Pain clearly teaches the making of chimereic chickens using embryonic stem cells. Petite teaches veterinary pharmaceutical formulation comprising genetically modified undifferentiated avian embryonic stem cells. Thus it would have been obvious to one ordinary skill in the art at the time the instant invention was made. to modify the teaching of Pain with Petite and Gibbins by substituting the embryonic stem cells with genetically modified avain embryonic stem cells in order to make chimeric chickens.

In response to applicant's argument that one would not have a reasonable expectation of success, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In instant case Pain and Petite clearly teaches culture conditions for long-term maintenance of avian embryonic stem cells (at least 19 days). In addition Petite and Gibson clearly teaches genetic modification of embryonic stem cells using viral or non-viral vectors in order to make chimeric birds. Thus a chimeric chicken made by substituting the embryonic stem cells with genetically modified stem cell is obvious in view of Pain, Petite and Gibbins.

Furthermore the chimeric bird (product) as claimed is indistinguishable from the chimeric bird as suggested by the combined teaching of cited prior art of record because if the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). In instant case the chimeric chicken (as claimed) is indistinguishable from the cited art of record, since one skill in the art would NOT be able to differentiate the chimeric chicken as claimed from the chimeric chicken disclosed in the prior art of record. The genome of the chicken embryonic stem cells would be same even after long-term culture of 160 days, while maintaining the expression of antigens characteristic of chicken ES cells (see Pain page 2343 col.2). Thus the invention as claimed is obvious over the cited prior art of record.

### **Conclusion**

Claims 41-50 are allowable.

Claims 21 and 26-30 are rejected.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the




shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547**. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**

  
**SUMESH KAUSHAL**  
**PRIMARY EXAMINER**  
**ART UNIT 1633**